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Ablation of Atrial Fibrillation in the Rapid Pacing Canine Model Using a Multi-Electrode Loop Catheter

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OBJECTIVES This investigation details our experience using a loop catheter to ablate atrial fibrillation (AF) in dogs.

BACKGROUND Atrial fibrillation is the most common arrhythmia and has significant morbidity. Maintenance of normal sinus rhythm (NSR) after conversion in many patients is still a challenge.

METHODS A multi-electrode loop catheter was used to create linear atrial lesions to ablate AF in a rapid atrial pacing model in 29 dogs. Rhythm status was assessed over a six-month recovery period, after which tissue analysis was performed.

RESULTS Acute conversion to NSR or atrial tachycardia (AT) was achieved in 90% of cases. Six of 26 conversions occurred after only left atrial (LA) lesions, and two after just right atrial lesions. Sixteen (62%) of 26 lesions that resulted in AF conversion were in the LA, and 11 of these 16 conversions occurred during a lesion connecting the mitral ring to the pulmonary veins. Acute conversion rate was similar with ring and coil electrodes, but AT was more frequent with coil electrodes (63% vs. 31%). At six months 80% of dogs were in NSR, 14% were in AT, and 7% remained in AF. There was an average reduction in P-wave amplitude of 64 ± 26% after power application. Tissue analysis revealed transmural contiguous lesions when final outcome was NSR, and nontransmural/noncontiguous lesions where AF persisted.

CONCLUSIONS Multi-electrode loop catheters can create contiguous transmural lesions in either atrium to safely and effectively ablate AF and provide a stable long-term rhythm outcome in this dog model. The left atrium appears to be the dominant chamber that sustains AF. Atrial tachycardia is a frequent acute outcome with coil electrodes. (J Am Coll Cardiol 2001;37: 1733–40) © 2001 by the American College of Cardiology

Currently, the maze operation is the most effective treatment for atrial fibrillation (AF), with a long-term success rate of over 90% in selected series (1). In recent years there has been increased interest in the use of ablation to replace surgical therapy for arrhythmias. A percutaneous transvascular catheter approach to ablate AF by separating atrial tissue with linear radiofrequency (RF) lesions, if effective even in a selected patient population, would be a significant achievement in the treatment of this highly prevalent disorder.

This manuscript summarizes our experience with RF ablation of AF induced by rapid atrial pacing in dogs. Ablation was performed with a loop catheter technology that was specifically designed to enable the creation of contiguous transmural linear lesions in the right (RA) and left atrium (LA) (2). The catheters were equipped with one of two types of electrode sets: ring or coil electrodes. The goal of this study is to define the efficacy and safety of the loop catheter design for the creation of contiguous linear lesions to ablate AF.

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METHODS

All procedures were performed in compliance with the American Heart Association's guidelines for animal research and were approved by the Animal Care Committee of the University of Illinois at Chicago. Twenty-nine adult male mongrel dogs, weighing 32 ± 5 kg, were used.

Rapid atrial pacing AF model. Chronic AF was induced by dual-site rapid atrial pacing. Two bipolar screw-in J leads (Pacesetter, Cardiac Rhythm Management Division, Sylmar, California) were implanted. One was fixed in the low RA and the other was placed in the RA appendage. The leads were connected to a custom-made pacemaker (Pacesetter).

After 24 h, the pacemakers were programmed to stimulate the RA appendage at 400 beats/min. The low RA was paced with every fourth RA appendage pacing stimulus. Each week the pacemakers were turned off, surface electrocardiograms were obtained and telemetry was used to examine atrial activity. Sustained AF developed within 45 ± 43 days. Rapid atrial pacing was continued for a total of 104 ± 69 days. The rapid pacing was stopped, and sustained AF was present for 202 ± 80 days.

The loop catheter and AF ablation system. Two loop catheters (BSC/EP Technology, San Jose, California) were evaluated (Fig. 1). The first is 8F and is equipped with twenty-four 4-mm ring electrodes spaced 4 mm apart. In

Abbreviations and Acronyms

AF	=	atrial fibrillation
AT	=	atrial tachycardia
CS	=	coronary sinus
LA	=	left atrium
MV	=	mitral valve
NSR	=	normal sinus rhythm
ODAT	=	overdrivable atrial tachycardia
PV	=	pulmonary vein
RA	=	right atrium
RF	=	radiofrequency
SAT	=	sustained atrial tachycardia

these catheters a thermistor was placed at the center of each ring electrode for temperature control. The second design employs fourteen 12-mm-long coil electrodes spaced 2 mm apart. When RF power is applied through the ablation electrodes the current density is highest at the edges (3). Therefore, in this catheter thermistors were placed at the edges of each coil electrode.

The catheters can be introduced via 9.5F 70-cm pre-curved guiding sheaths designed to allow placement of the catheter in pre-specified locations (Fig. 1). Because atrial chambers are globular and elastic, expansion of the loop catheter forces its electrodes into dynamic contact with atrial tissues, which is essential for the creation of contiguous transmural lesions with RF power.

Linear lesion creation. ANESTHESIA AND MAINTENANCE. Anesthesia was induced with propofol (7 cc/kg) and maintained with a mixture of halothane (1.5%) and oxygen. The dogs were ventilated at 12 breaths/min at a tidal volume of 15 ml/kg.

CATHETER PLACEMENT AND CHAMBER ELECTRICAL ACTIVITY. Quadripolar 6F catheters were placed in the high RA and coronary sinus (CS) via the external jugular vein. Bipolar local electrical activity was recorded from the RA and LA via the high RA and CS catheters, respectively, on an electrophysiology monitoring system (Prucka Engineering, Houston, Texas). The femoral vein was cannulated with a self-sealed 14F short access sheath. A guiding sheath was inserted via the access sheath. For LA placement, transeptal cannulation was achieved under transesophageal echocardiographic guidance via the Brockenbrough technique.

LESION LOCATIONS. Five targets were selected for lesion placement based upon the maze procedure, the need to create a lesion around the pulmonary veins (PVs) and the mechanical characteristics of the loop catheters that cause them to adapt to the maximal circumference within a globular chamber. Each repositioning of the catheter was counted as a linear lesion. The lesions were created in a variety of sequences at the four positions as noted in Figure 2.

LESION CREATION PARAMETERS (TEMPERATURE, IMPEDANCE, AND POWER MONITORING). Radiofrequency power was applied sequentially through each electrode. With the ring electrodes, RF power was delivered up to a maximum of 50 W for 60 to 80 s. Ablation efficacy was assessed during power application by viewing changes in the amplitude and character of the local electrograms and by monitoring the temperature (with a target of 70°C), power and impedance. Power delivery was manually stopped if a rapid impedance rise occurred. With the coil electrodes, RF power was

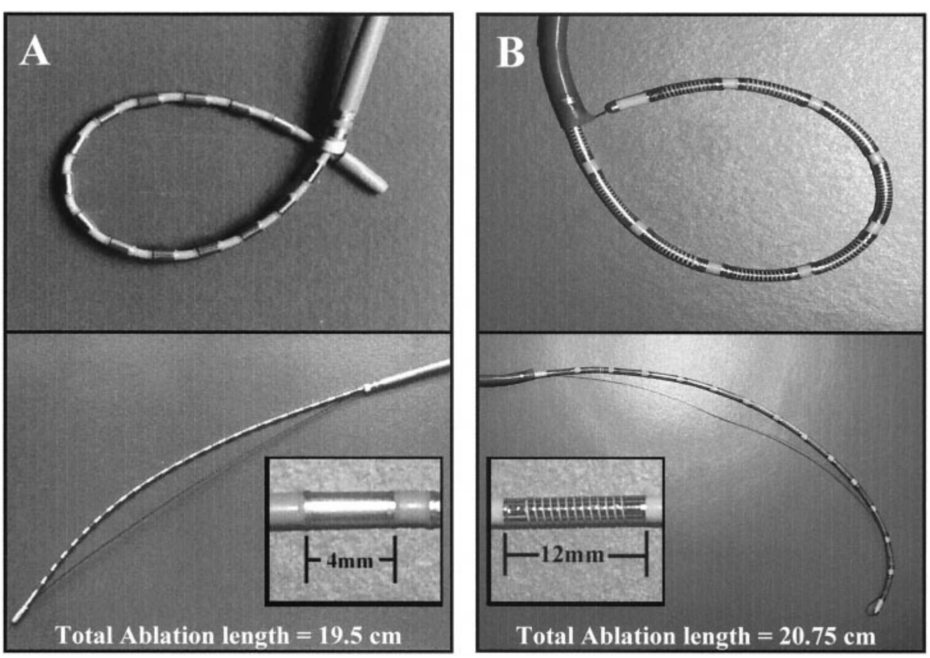


Figure 1. The loop catheter system. **(A)** 8F with twenty-four 4-mm-long ring electrodes spaced 4 mm apart. **(B)** 8F with fourteen 12-mm-long coil electrodes spaced 2-mm apart. A soft, braided pull wire attached to the distal tip of the catheter can be retracted into the long guiding sheath to deflect the catheter tip to create a loop of various sizes.

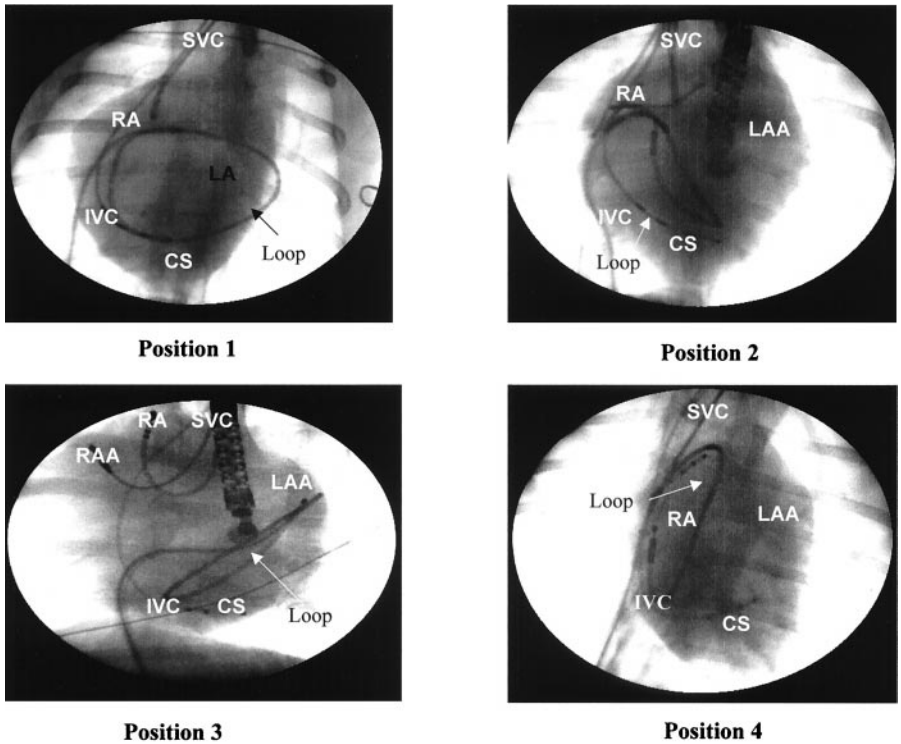


Figure 2. Fluoroscopic images of catheter positions for linear lesion creation. These fluoroscopic panels presented in the posteroanterior position of the C arm, showing the loop catheter deployed in the right atrium (RA) and left atrium (LA) in the positions where linear lesions were created. Standard high-RA and coronary sinus (CS) catheters and a transesophageal echocardiography probe are visible in some of the panels. **(Position 1)** Lesion encircling the pulmonary veins (PVs). The posterior portion of the circle is close to the mitral valve (MV) ring, as shown by the proximity of the loop to the CS catheter. The anterior segment is located under the left and right superior PVs. **(Position 2)** Left atrial circular lesion extending from the medial portion of the MV ring to the lateral wall of the LA. **(Position 3)** Left atrial circular lesion connecting the lateral portion of the MV ring and the superior portion of the atrial septum. **(Position 4)** Right atrial circular lesion from the inferior vena cava (IVC) across the isthmus, to the anterior septal region of the tricuspid valve ring, to the RA appendage (RAA), to the superior vena cava (SVC) and back to the IVC. LAA = LA appendage.

delivered by a generator (EPT Model 1000XP, BSC/EP Technology, San Jose, California) that delivered a maximum of 150 W under automatic closed-loop temperature control. The maximum temperature was set at 70°C with RF current limited to 0.9 A. Temperature, power, impedance and current were continuously recorded on a dedicated PC during each power application.

P-WAVE DIMINUTION. In eight dogs (four rings and four coils), a total of 438 individual RF applications were performed where the rhythm status was AF before and after RF power application. For these RF applications, the diminution in P-wave amplitude after ablation was averaged for a 5-s interval using a software caliper. The P-wave reduction for each dog was averaged and the differences were analyzed using each dog as a unit of analysis.

RECOVERY AND MONITORING. Fifteen dogs were monitored for 227 $\pm$ 53 days after ablation with electrical activity assessment every two weeks. A final study was performed six to eight months after ablation to evaluate the rhythm outcome. The initiation of atrial arrhythmia with premature beats was attempted via a high RA catheter with basic cycle lengths of 400, 350 and 300 ms and the initiation of a premature stimuli every eighth pacing pulse starting at 280 ms and decremented by 20 ms down to 200 ms. Atrial arrhythmia induction was also evaluated with 10 attempts of burst pacing at 50 ms cycle length for 5 s.

GROSS AND HISTOPATHOLOGIC EVALUATION. At the conclusion of the final study, the hearts were excised and examined for structural abnormalities. The integrity of the foramen ovale, mitral and tricuspid valves was assessed. The atria were isolated and immersed in tetrazolium blue stain for 24 h, after which the gross characteristics of the lesions were documented. Histologic lesion sections were obtained from eight dogs by dissecting the atria along the midline of the lesions. Tissues were stained with hematoxylin and eosin stain and trichrome stain, and light microscopy was used to evaluate lesion contiguity and transmurality, calcification and fibrous tissue formation.

Statistical analysis. Summary data are expressed as mean value $\pm$ one standard deviation. The unpaired *t* test was used to compare parameters (such as temperature, power and impedance) between ring and coil groups of dogs. Differences in P-wave amplitude reduction after ablation versus preablation in both atria between coil and ring electrodes were analyzed with two-way repeated-measures analysis of variance. The number of dogs used was eight (the dog was used as the unit of analysis). The null hypothesis was rejected at the level of $p < 0.05$.

Table 1. Acute and Six-Month Rhythm Outcome After Linear Lesions

Rhythm	Rings		Coils		Combined	
	Acute (n = 13)	Six Months (n = 4)	Acute (n = 16)	Six Months (n = 11)	Acute (n = 29)	Six Months (n = 15)
NSR	8 (61%)	4 (100%)	4 (25%)	8 (73%)	12 (41%)	12 (80%)
ODAT	1 (8%)		6 (37%)	1 (9%)	7 (24%)	1 (7%)
SAT	3 (23%)		4 (25%)	1 (9%)	7 (24%)	1 (7%)
AF	1 (8%)		2 (13%)	1 (9%)	3 (10%)	1 (7%)

AF = atrial fibrillation; NSR = normal sinus rhythm; ODAT = overdrivable atrial tachycardia; SAT = sustained atrial tachycardia.

RESULTS

Linear lesion generation. A total of 180 linear lesions were placed in 29 dogs (6 ± 3 lesions per dog). The ring electrode catheter was used in 13 dogs and the coil electrode catheter was used in 16 dogs. The initial lesion was placed in the LA in 15 dogs.

Rhythm outcomes (acute and at six months). The rhythm outcomes are shown in Table 1. In 26 (90%) of 29 dogs, AF was converted to normal sinus rhythm (NSR) or atrial tachycardia (AT) after 5 ± 2 lesions (3 ± 2 LA lesions and 2 ± 2 RA lesions). Only three (10%) dogs remained in AF (four, seven and nine total lesions, respectively). At the end of the procedure, 12 (41%) dogs maintained NSR despite attempts to induce arrhythmia. In 14 (48%) cases AT could be induced, and in seven of these the AT could be converted to NSR via overdrive pacing.

Of the 15 dogs that were followed for six months after ablation, NSR was maintained in 12 (80%). One developed overdrivable AT (ODAT) after exhibiting NSR immediately after ablation. Three of the four dogs with acute ODAT maintained NSR at six months, while one developed sustained AT (SAT). Both dogs with acute SAT were in NSR after six months.

Atrial fibrillation was persistent throughout in one dog, despite seven linear lesions. There was no incidence of new AF during the follow-up period.

RING VERSUS COIL CATHETERS. The conversion rate to either NSR or AT was similar with the use of rings (92%) and coils (87%). However, NSR was achieved in only 25% of the coil electrode ablations versus 61% with ring electrodes. The acute conversions were more likely to be to AT with coil electrodes (10 of 16 vs. four of 13). Six of the ten conversions to AT using coil electrodes were to ODAT, while one of the four conversions to AT with ring electrodes was overdrivable (Table 1).

Ablation targets. SPECIFIC ATRIUM-CONVERTING AF. Eighteen (69%) of 26 conversions occurred after creating lesions in both atria. Of the eight conversions that occurred after ablating in a single atrium, six were achieved after generating only LA linear lesions (five converted to SAT and one to NSR). The two conversions achieved with lesions placed only in the RA were to SAT and to NSR. In the three cases where AF was not converted, lesions were created in both atria.

SPECIFIC LESION CONVERTING AF. In 16 (62%) of 26 AF-converting lesions the lesion was located in the LA, 10 conversions occurred with the catheter extending from the mitral valve (MV) ring to the superior PV and six occurred with the catheter positioned around the PVs (position 1). Twelve conversions occurred after a lesion located below the PVs and another lesion connecting the MV ring to the PV.

In 20 cases the conversion from AF was to AT. Thirteen (65%) conversions from AF to AT occurred during a lesion in position 1. In nine (69%) of these cases lesions in positions 1 and 2 were the specific converting lesion. Of the six conversions from AF to NSR, half occurred after a lesion in the LA (two in position 1 and one in position 2) and the remaining three converting lesions were in position 4.

Rhythm organization and electrical isolation. In many cases a series of organizational events were observed as the activity was converted from AF to AT and from AT to NSR (Fig. 3). There were 39 occasions where organization to SAT, ODAT or NSR occurred. These events most often occurred after lesions had been created in both atria (30 of 39). There were nine instances where organizations occurred after lesions in a single atrium, and six of these events were after LA lesions. Seven cases of organization to ODAT occurred after creating lesions in both atria.

In five of 29 dogs, regional electrical isolation was recorded in the LA involving the distal CS and the tissues under the left superior PV (Fig. 4). The tissue isolation involves the completion of lesions in positions 1 and 2 or 3 that disconnect the distal CS from the atria.

RF ablation parameters. The average temperature was not significantly different between the ring (294 individual RF applications in four dogs) and coil (373 individual RF applications in four dogs) electrode catheters (62.9 ± 11.1 vs. 60.5 ± 11.4°C, respectively; $p > 0.05$). For the coil catheter, the power required to maintain temperature was significantly greater and the impedance was significantly smaller (power: 27.4 ± 9.8 vs. 21.1 ± 11.8 W, $p < 0.05$; impedance: 91.8 ± 17.5 vs. 131.2 ± 27.8 ohms, $p < 0.05$).

P-wave diminution. In eight dogs, the rhythm status was AF before and after RF power application. There was an average reduction in P-wave amplitude of 64 ± 26% after power application. With ring electrodes, the P-wave reduction was significant in both atria (RA: 0.78 ± 0.31 vs. 0.36 ± 0.13 cm, $p < 0.05$; LA: 1.45 ± 0.34 vs. 0.39 ±

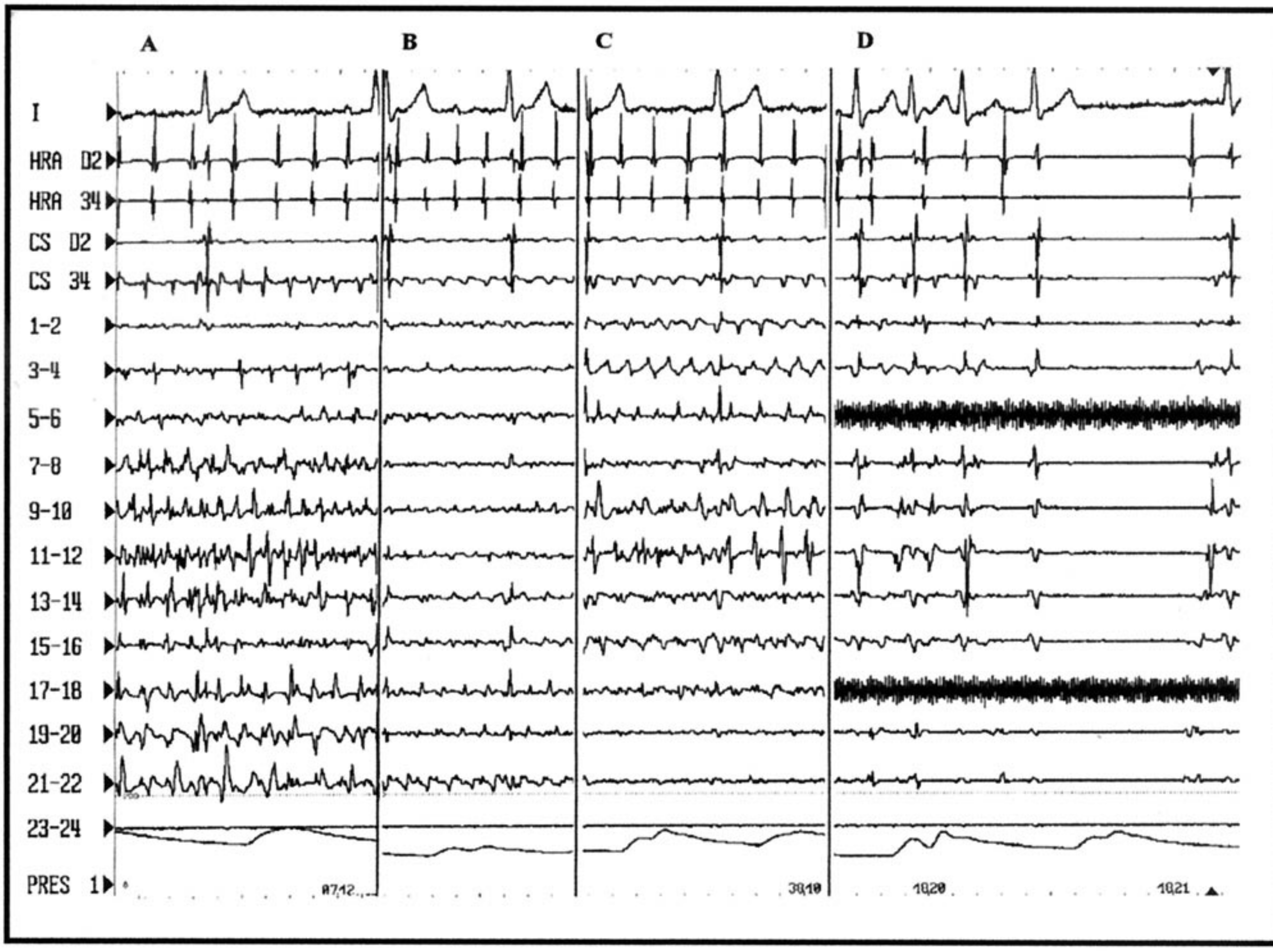


Figure 3. Organization of the electrical activity before and after lesion creation. In many cases as linear lesions were created the local atrial electrical activity progressively organized to the point of conversion to normal sinus rhythm (shown on **panel D** during lesion creation in position 2). **Panel B** depicts the marked reduction in the local electrical activity amplitude as a result of the lesion created in position 1 when compared with the preablation recordings shown in **panel A** (all the recordings are bipolar: 1 and 2, 3 and 4, etc.). HRA = high right atrium; CS = coronary sinus; 1 to 24 = ring electrodes.

0.13 cm, $p < 0.01$). However with coil electrodes, P-wave reduction was statistically significant only with the lesions created in the LA (LA = 0.22 ± 0.06 vs. 0.12 ± 0.02 cm, $p < 0.05$; RA = 0.30 ± 0.12 vs. 0.14 ± 0.08 cm, p = NS). Overall, the reduction of the P-wave amplitude was more significant in the burns using the ring electrodes in comparison to the coil electrodes (difference of P-wave amplitude postablation vs. preablation was 0.61 ± 0.43 cm in rings and 0.12 ± 0.11 cm in coils; $p < 0.01$).

Tissue analysis. Examples of gross and histologic tissues obtained six months after ring ablation are shown in Figure 5.

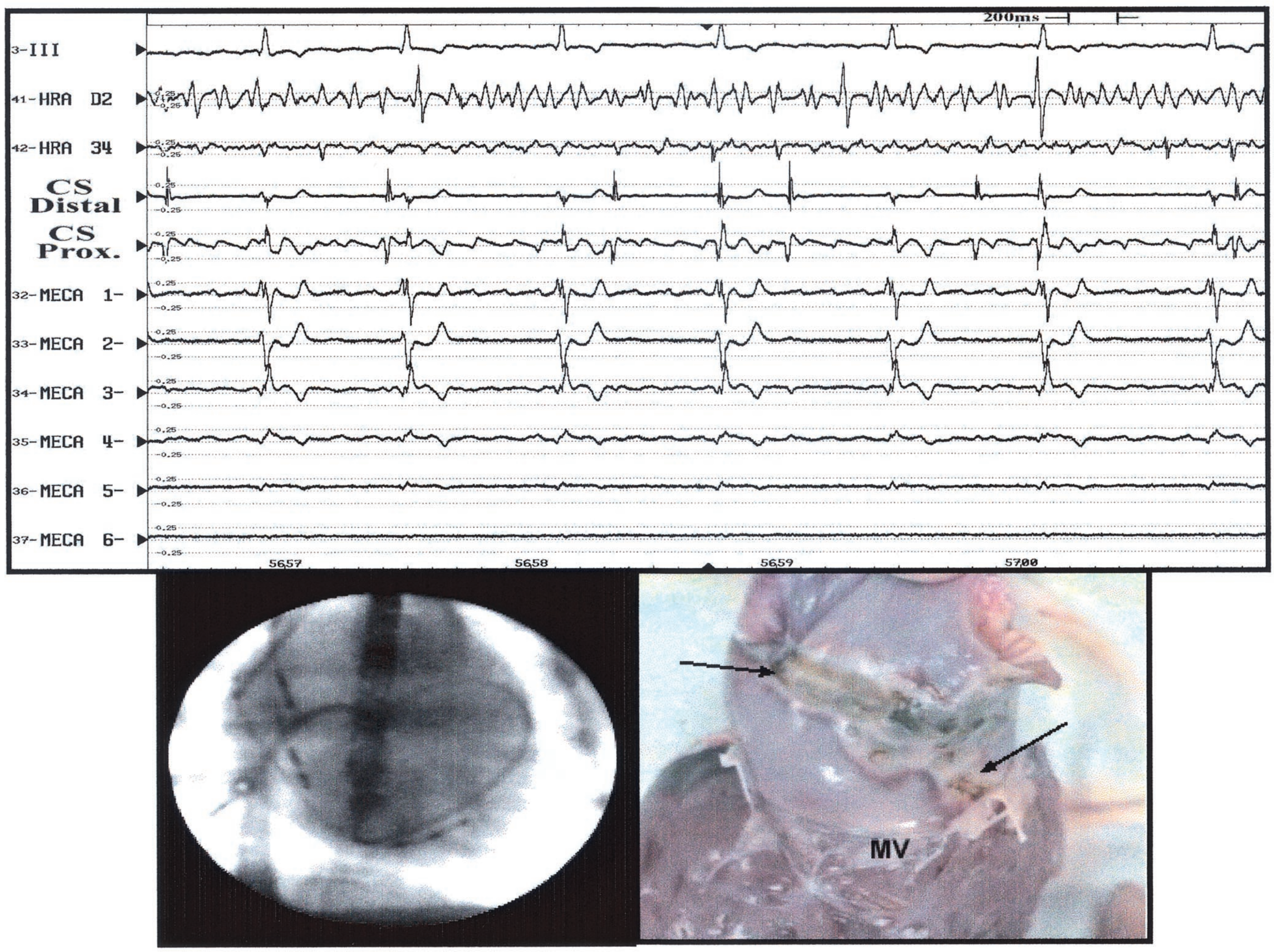
GROSS PATHOLOGY. In all cases the mitral and tricuspid valve leaflets and chordae were intact and the atrial septum puncture was sealed. None of the dogs had LA or RA thrombus. The endocardial surface was fully healed, with palpable elevated lesions that were up to 19 cm long and 8 mm wide with a total LA lesion area of 12 to 15 cm^2. Although large portions of the lesions consisted of fibrous tissues, calcification was palpated and observed under light microscopy in many of the lesions.

HISTOLOGY. Microscopic evaluation of the linear lesions was performed in eight cases, of which the six-month rhythm outcomes were NSR (four), AF (three) and SAT (one). All of the lesions in the four NSR dogs were transmural and contiguous. One of the three AF dogs had a noncontiguous and nontransmural region in the LA septum. The second dog had two noncontiguous and nontransmural lesions, one in the region of the superior vena cava to inferior vena cava and another connecting the MV ring with the PV. The third dog had three noncontiguous and nontransmural lesions: at the SVC to the tricuspid ring junction, at the LA septum and in a lesion connecting the MV ring with the base of the LA appendage (the lateral segment of the lesion in position 1). The dog with SAT had nontransmural lesion in the RA.

DISCUSSION

Much attention has been directed at creating long linear lesions to convert AF on the basis of the surgical maze procedure (1). Although a focal source may be the etiology of AF in some cases (4), the maze procedure neglects

A



B C

Figure 4. Example of distal coronary sinus (CS) electrical isolation from the rest of the atria after linear lesions in positions 1 and 3. **(A)** Recordings showing distal CS isolation from the rest of the right atrium. **(B)** The loop catheter in position 1. The posterior portion of the circle is close to the mitral valve ring, as shown by the proximity of the loop to the CS catheter. The anterior portion is under the superior pulmonary veins. **(C)** Lesion gross pathology in the left atrium (arrows = lesions). The recordings in the high right atrium (HRA) and proximal CS between electrodes 1 and 2 are atrial fibrillation, but the distal CS recordings between electrodes 3 and 4 show sporadic depolarization. III = electrocardiogram surface lead; MECA = multi-electrode catheter ablation system bipolar recordings betweenelectrodes 1 and 2, 2 and 3, etc.

discrete focal lesions and instead creates atrial compartmentalization through incision and cryosurgery. Linear lesions have been placed in animals to successfully ablate AF induced by methacholine infusion (5,6), vagal stimulation with burst pacing (6), sterile pericarditis, mitral regurgitation (7) and long-term rapid atrial pacing (7–10). None of the animals in these studies were allowed to recover for six months after lesion creation. Our study has demonstrated that linear lesions created with a multi-electrode loop catheter in a rapid atrial pacing model of AF can achieve acute conversions in 90% of cases and the rhythm remains stable for six months after ablation.

In many of these dogs the AF was converted to AT, which was often overdrivable to NSR. Almost all dogs that had inducible AT immediately after ablation exhibited NSR after six months of recovery. Only one dog had a new onset of ODAT one month after ablation, and there were no cases with a new onset of AF during the recovery period.

The primary goal of AF ablation is the conversion to NSR. In this study, a high rate of conversion to AT was recorded acutely, most commonly with the coil electrode technology. The outcome differences can be attributed to the transmurality and contiguity of the lesions. In the dogs that were converted to NSR, histologic analysis revealed transmural contiguous lesions. In the dogs with AT and AF, lesions were nontransmural or noncontiguous and the reduction in local electrical activity with the ring electrodes was significantly greater compared with the coil electrodes, suggesting more complete tissue destruction (2).

Although AT was induced in many dogs, only one

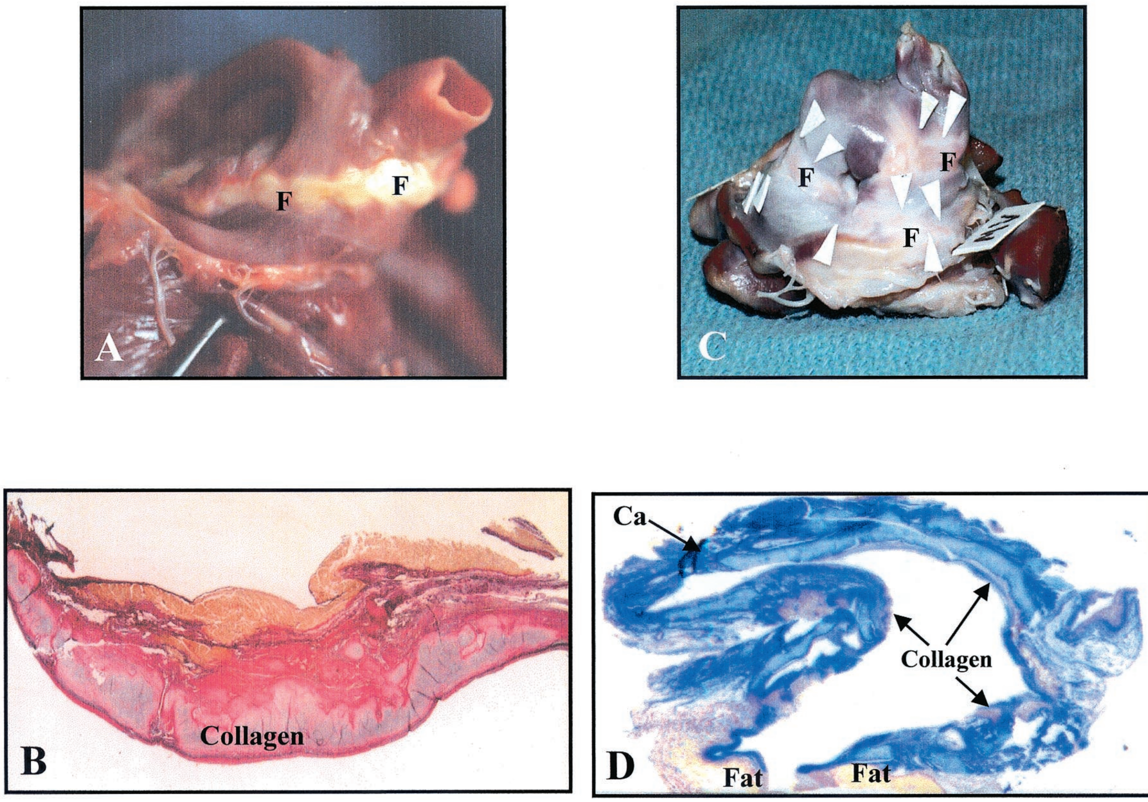


Figure 5. Gross pathology and histology of ring versus coil lesions. **(A and B)** Healed radiofrequency lesions in position 1 created with the 4-mm ring electrode loop catheter. **(C and D)** Linear lesions created with the 12-mm coil electrode loop catheter. The 4-mm lesion is elevated and visibly defines each of the ring electrodes, whereas the 12-mm coil electrode lesions are flat. The histologic sections exemplify contiguous and transmural linear lesions. Collagen formation can be seen on both histologic panels. F = fibrous tissue; Ca = calcium deposition.

manifested AT after six months. The potential for incessant AT is a major concern because ventricular rate control with this atrial rhythm is likely to be more difficult than with AF. Furthermore, ablation of AT will require precise mapping of atrial activity, which in turn requires additional hours of LA instrumentation and may subject the patient to the risk of stroke. It is possible that the AT that was noted acutely after ablation is a transient phenomenon, as has been documented in humans after cardiac surgery (11).

Ablation targets. Several investigations have documented that the LA is often the source of AF in humans (12,13). This also appears to be true in the rapid atrial pacing model (8). Of the 26 conversions achieved in our study, six were after lesions that were created in the LA alone; however, in two cases conversion occurred after only RA lesions. An encircling lesion connecting the MV ring to the PVs was the most common converting lesion. The conversion to NSR from AF is often a sequential process of organization in atrial activity, suggesting a reduction of the number of reentrant wavelets (7).

Although we hypothesize that the AF induced in this model is caused by electrical remodeling as well as cellular changes (9) that result in the formation of multiple wavelets (14,15), we cannot exclude the possibility that the AF is a result of depolarization activity of cells within a region or regions that were not ablated or isolated by linear lesions. Furthermore, no attempt was made to isolate the PVs and none of the lesions were placed in the PV. Thus, it is unlikely that cells within the PV are active participants in the maintenance of AF in this model. We cannot exclude the possibility that pacemaker cells within the atrial tissues might have been ablated in the successful conversions and might have survived in the failed ablations.

The documented cases of regional electrical isolation testify to the ability of this technology to create contiguous transmural lesions. Isolation of the CS is not an undesirable outcome and may not affect the atrial mechanical function. However, the isolation of other LA tissues may result in a significant impact on atrial function and increase the possibility of stroke.

Local electrical activity and tissue analysis. There were three cases where a conversion from AF could not be achieved despite linear lesions in both atria. This may be attributed to inappropriate lesion location or failure to create contiguous transmural lesions. It is possible that nontransmural lesions were responsible for the high incidence of atrial arrhythmias after ablation. This finding is supported by other investigations that have documented conduction through gaps of surviving tissue in incomplete linear lesions (16) and their correlation to atrial flutter.

The local electrical activity diminution after ablation has been shown to indicate tissue ablation (2). In this study significantly greater reduction of local electrical activity was noted after ablation with the ring ablation electrode, which paralleled with a lower rate of AT induction. The conversion rate from AF was similar with the ring and coil electrodes, but the acute conversions with coil electrodes were more likely to have overdrivable AT. This effect might be due to the differences in power distribution between the electrodes. With 12-mm coil electrodes, there is greater heat generated at the edges of the electrodes (3). This uneven heat dispersion may allow conductive gaps to remain in the ablated tissue at the center of the electrode. It is possible that a higher heating temperature may increase lesion contiguity and transmurality with the 12-mm coil electrodes, but such a temperature must be proven to be safe, without causing impedance rises and increasing risk of stroke.

Conclusions. This multi-electrode loop catheter can create contiguous and transmural lesions in either atrium to safely and effectively ablate AF and provide a stable six-month rhythm. The LA is usually the most likely to result in AF conversion in this chronic rapid atrial pacing dog model. The small percentage of cases where ablation fails are likely due to nontransmural lesions in the left atrium. Successful conversion from AF is equally likely with 4-mm ring electrodes and 12-mm coil electrodes, although atrial tachycardia is more likely to be present acutely after ablation with 12-mm coil electrodes.

This technology can be effective in ablating atrial fibrillation in humans with reduced procedure times and radiation exposure.

Study limitations. The results in this study were obtained in a dog model that may not simulate AF in humans, which is caused by a wide spectrum of pathology. However, the chronic nature of this model along with the development of mitral regurgitation and LA expansion correlates with the presentation of AF in humans. Although the creation of linear lesions resulted in AF conversion in 90% of the dogs, successful conversion was not assured.

Other potential limitations of this technique include: 1) the inability to provide simultaneous RF delivery throughout the whole electrode surface in contact with the target tissue, particularly in close contact with anatomical holes (orifices of caval and PVs, CS and tricuspid and mitral annuli); 2) the potential danger of thromboembolic risk, which was not evaluated in this study; 3) the high dependency of lesion geometry on the catheter loop configuration.

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